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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,850	12/14/2001	Patrick M. Hughes	D-3004	7435

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STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA 92618

EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 02/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/016,850	Applicant(s) HUGHES ET AL.	
	Examiner Phyllis G. Spivack	Art Unit 1614	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 January 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet.* (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-6,8,9 and 11-16*.
   Claim(s) withdrawn from consideration: *7 and 10*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
    In response to Applicants' assertion that the Examiner agrees ophthalmic conjugates are enabled, the Examiner acknowledges only enablement for ophthalmic drops, not for any ophthalmic product or conjugate. In view of the plethora of functionalities encompassed in the recitation "a therapeutic component", the rejection under 35 U.S.C 112, first paragraph, for lack of enablement, is maintained as set forth.

Applicants' argument in response to the rejection of record under 35 U.S.C. 103 is not persuasive. Applicants urge motivation to combine the two references is absent. A conjugate is no more than a combination of compounds wherein increased solubility or bioavailabity for poorly soluble drugs is sought. One skilled in the art of formulation chemistry would have been motivated to prepare conjugates of various therapeutic agents in view of the prior art. Desantis teaches brimonidine to be well known in the prior art as an antiglaucoma agent and memantine is a compound of instant formula A. Collins teaches the known utility of conjugates as pharmaceutical formulations wherein a low molecular weight linker is covalently bound to a bioactive agent. In view of the prior art references, one skilled in the art of formualtion chemistry would have been motivated to prepare an ophthamic pharmaceutical conjugate comprising brimonidine, memantine and, optionally, a linker, with a reasonable expectation of improving bioavailability of the therapeutic agent.

12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

U.S. Patent and Trademark Office
PTOL-303 (Rev. 9-04)

Advisory Action Before the Filing of an Appeal Brief

Part of Paper No. 021305

Continuation of 3. NOTE: The amendment to claims 1 and 16 raises new issues requiring further consideration and search. The amendment intoduces the requirements that the pharmaceutical conjugate is ophthalmic and that the efficacy enhancing component is effective in delivering the conjugate to a posterior portion of an eye when topically administered.

Continuation of 5. Applicant's reply has overcome the following rejection(s): the rejection of claims 1-6, 8, 9 and 11-16 under 35 U.S.C. 112, second paragraph, and the rejection of claim 8 under 35 U.S.C. 112, both first and second paragraph.

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

13 February 2005